PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 2002.015 WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/10189	International filing date *(day/month/year)* 11.09.2003	Priority date *(day/month/year)* 13.09.2002
International Patent Classification (IPC) or both national classification and IPC C07K16/18		
Applicant UNIVERSITEIT GENT et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24.03.2004	11.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Griesinger, I Telephone No. +49 89 2399-7596

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/10189

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-41 as originally filed

Sequence listings part of the description, Pages

1-27 as originally filed

Claims, Numbers

1-8 received on 11.10.2004 with letter of 07.10.2004

Drawings, Sheets

1/11-11/11 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☒ contained in the international application in written form.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

   ☒ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☒ complied with.

   ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-8
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-8
Industrial applicability (IA)	Yes:	Claims	1-8
	No:	Claims	

2. Citations and explanations

   see separate sheet

1. Introduction

The international preliminary examination report refers to the following documents (D) cited in the international search report:

D1: Entry in the EMBL database, accession number AJ310819
D2: WO9509182
D3: VERCAUTEREN ISABEL ET AL: "Identification of excretory-secretory products of larval and adult Ostertagia ostertagi by immunoscreening of cDNA libraries." MOLECULAR AND BIOCHEMICAL PARASITOLOGY. NETHERLANDS FEB 2003, vol. 126, no. 2, February 2003 (2003-02), pages 201-208, XP001156729 ISSN: 0166-6851

The present application relates to immunogenic proteins of Ostertagia ostertagi, and in particular to a protein according to Seq. ID No. 8 with a molecular weight of >200kD and the corresponding nucleic acid sequence according to Seq. ID No. 7. Said protein was deduced from a cDNA sequence, wherein the cDNA sequence was identified by screening a cDNA library with antibodies. Said antibodies were either 1) in the form of polyclonal serum of rabbits immunized with excretory-secretory (ES) products of the nematode (example1) or 2) local antibodies obtained from mucus and antibody secreting cell (ASC) culture supernatant (example 3).

D1 discloses the nucleic acid sequence of an EST which is 100% identical over the full length to the sequence according to Seq. ID No. 7 of the present application. The EST is derived from excretory-secretory products of Ostertagia ostertagi.

D2 relates to antigenic peptides of 26-36kDa and 91-105kDa of a complete L3 larvae of Ostertagia circumcincta. The peptides were identified by Western blotting and short stretches of the peptides were sequenced. The proteins are intended to be used as vaccines.

D3 was published prior to the international filing date but later than the priority date claimed (PX document). Said document is not considered when accessing novelty and inventive step, since regulations concerning such "PX" documents differ between the PCT member states. However, the document may be relevant for accessing novelty and inventive step of the present application during regional and national proceeding. In any case, the document is relevant for accessing credibility of the subject-matter claimed. This is particulary true, since it seems to be the scientific publication

corresponding to the application.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of all claims does not involve an inventive step in the sense of Article 33(3) PCT.

1. The subject-matter of claims 1 and 2 is not inventive in view of D1 alone or in combination with D2 for the following reasons.

Claims 1 and 2 relate to first and further medical uses of a protein having at least 90% "homology" to the sequence according to Seq. ID No. 8 or immunologic fragments thereof, wherein said uses are the use of the protein in a vaccine. However, the present application does not seem to provide evidence that the protein has protective capacities against Ostertagia ostertagi infection: Said protein was deduced from cDNA sequence, wherein the cDNA sequences were identified by screening a cDNA library with multiple different antibodies. Consequently, it is only shown, that said protein is recognized by antibodies, i.e. it is an antigen. However, a protein to be useful as a vaccine, needs to activate the immune system beyond induction of antibodies alone, namely the protein must trigger the host's immune response to effectively interfere with the course of an infection or disease. No evidence is provided for such a protective capacity of the protein claimed. The PX document D3, which seems to be the scientific publication corresponding to the present application, also emphasizes that the identified protein is one of the "proteins with *potential* protective capacities, which are *targets* for vaccine *development*" (see Abstract, last sentence, emphasize added by the examining division), i.e. it's usefulness in a vaccine was not yet shown.

Hence, the objective problem has to be reformulated as the provision of an antigen which is *potentially* useful for the preparation of a vaccine.

The solution, namely the provision of the protein according to Seq. ID No. 8 and of the corresponding "homologous" sequences and fragments, is obvious.

D1 already discloses the EST sequence encoding said protein and that the protein is a excretory-secretory product of Ostertagia ostertagi. It is general knowledge that most

secreted proteins of a pathogen are antigens which may be useful in a vaccine. Said general knowledge is confirmed by D2, which discloses that antigens of an Ostertagia species were identified with the intention to use them in a vaccine (see Abstract and claim 27). Consequently, the selection of the protein according to Seq. ID No. 8 must be considered to be an arbitrary selection from all proteins of Ostertagia with potential protective capacities. Therefore, the subject-matter of claims 1 and 2 is not inventive.

2. The same reasoning applies for vaccines comprising antibodies against the protein having at least 90% "homology" to the sequence according to Seq. ID No. 8 or immunologic fragments thereof, since no protective effect has been shown for said antibodies. Hence, the subject-matter of claim 4 is not inventive.

3. An inventive step may be acknowledged for first and second medical uses of the protein having at least 90% "homology" to the sequence according to Seq. ID No. 8 or immunologic fragments thereof and for antibodies against said proteins, if evidence was provided that the protein has protective capacities, i.e. is in fact useful for the preparation of a vaccine.

4. Claim 3 relates to a vaccine comprising the protein having at least 90% "homology" to the sequence according to Seq. ID No. 8 or immunologic fragments thereof. Said claim is interpreted as being directed to a product as such, which is suitable for the intended use as a vaccine. Consequently, claim 3 relates to a solution of the protein or it's fragment, which is suitable for use as a vaccine, i.e. to the protein or the protein fragments in water or buffer.

D1 already discloses a sequence encoding said protein, i.e. implicitely already discloses the protein. Since it is common practice to store proteins as a solution in water or buffer, the subject-matter of claim 3 is not considered to be inventive.

5. The same considerations as for claim 3 apply for claim 8, since the method steps of the "method for the preparation of a vaccine" are identical to the method steps for the preparation of a solution comprising the protein according to Seq. ID No. 8 or it's "homologous" or fragments. Consequently, the subject-matter of claim 8 is not inventive in view of D1.

6. The addition of an adjuvant or antigens of other organisms can not make the subject-matter of claims 3 and 4 inventive. Therefore, the vaccines according to claims 5-7 are obvious in view of D1.

7. Further comments: The subject-matter of claims 1 and 2 is not supported by the description (Article 6 PCT), since the protective capacity of the proteins or peptides is not creadible for the reasons indicated under item V, 1.